Supporting Information

Hofmann Rearrangement of Carboxamides Mediated by Hypervalent Iodine Species Generated in situ from Iodobenzene and Oxone: Reaction Scope and Limitation

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General. All commercial reagents were ACS reagent grade and used without further purification. NMR spectra were recorded at 300 and 500 MHz (^1H NMR) and 75 MHz (^13C NMR). Chemical shifts (δ) are reported in parts per million. GC-MS analysis was carried out with a HP 5890A Gas Chromatograph using a 5970 Series mass selective detector.
Preparation of benzylamine hydrochloride 3•HCl from 2-phenylacetamide 2 via Hofmann rearrangement.

\[
\begin{align*}
\text{2} & \xrightarrow{1) \text{Phl (1 mol-equiv), Oxone® (2 mol-equiv)}} \text{CH}_3\text{CN-H}_2\text{O (1:1), rt, 7 h}} \rightarrow \text{3-HCl} \\
\text{NH}_2\text{-HCl}
\end{align*}
\]

To a mixture of Oxone® (1.23 g, 2 mmol) and iodosobenzene (0.204 g, 1 mmol) in CH\textsubscript{3}CN/H\textsubscript{2}O (6 mL, 1:1, v/v), 2-phenylacetamide 2 (0.135 g, 1 mmol) was added under stirring at room temperature. The reaction mixture was stirred at room temperature for 7 h (the reaction was monitored by GC-MS). After completion of the reaction, the reaction mixture was filtered under reduced pressure. The insoluble residue (mainly containing inorganic salts) was washed with CH\textsubscript{3}CN (5 mL) and discarded. The combined filtrate was mixed with HCl (15 mL, 20% aqueous solution), and the mixture was washed with ether (10 mL) to remove all non-polar impurities. The aqueous layer was concentrated at reduced pressure to give a sticky solid, which was thoroughly dried in vacuum. Crystallization from ethanol-ether afforded 0.136 g (95%) of benzylamine hydrochloride 3•HCl as a slightly yellow crystalline solid, mp 253-255 °C (lit.\textsuperscript{1}, mp 258-260 °C). \textsuperscript{1}H NMR 300 MHz (CD\textsubscript{3}OD): δ 4.12 (br s, 2H, -CH\textsubscript{2}CH\textsubscript{2}), 7.40 -7.48 (m, 5H, Ph).

Preparation of (±)-α-phenylpropylamine 5 from 2-phenylbutyramide 4

\[
\begin{align*}
\text{CONH}_2 & \xrightarrow{\text{Phl (1 mol-equiv), Oxone® (2 mol-equiv)}} \text{CH}_3\text{CN-H}_2\text{O (1:1), rt}} \rightarrow \text{NH}_2 \text{5}
\end{align*}
\]

To the mixture of Oxone® (1.23 g, 2 mmol) and iodosobenzene (0.204 g, 1 mmol) in CH\textsubscript{3}CN/H\textsubscript{2}O (6 mL, 1:1, v/v), 2-phenylbutyramide 4 (0.163 g, 1 mmol) was added under stirring at room temperature. The reaction mixture was stirred at room temperature for 7 h (the reaction was monitored by GC-MS). After completion of the reaction, the reaction mixture was diluted with H\textsubscript{2}O (10 mL), and extracted with CHCl\textsubscript{3} (3x10 mL). The organic phase was separated, and dried over Na\textsubscript{2}SO\textsubscript{4} (anhydrous). Evaporation of CHCl\textsubscript{3} under reduced pressure afforded 0.115 g (85%) of (±)-α-phenylpropylamine 5 as a pale yellow oil. \textsuperscript{1}H NMR 300 MHz (CDCl\textsubscript{3}): δ 0.87 (t, J=7.5 Hz, 3H, -CH\textsubscript{2}CH\textsubscript{3}), 1.61 (br s, 2H, NH\textsubscript{2}), 1.67-1.72 (m, 2H, -CH\textsubscript{2}CH\textsubscript{3}), 3.80 (t, J=6.9 Hz, 1H, -CH\textsubscript{2}-), 7.31-7.33 (m, 5H, Ph). The product was identical to a commercially available sample (Aldrich) according to NMR and GC-MS data.
General procedure for preparation of carbamates 7a-k from amides 6a-k via Hofmann rearrangement.

\[
R - ONH_2 \xrightarrow{\text{Phl (1 mol-equiv), Oxone (2 mol-equiv)}} \xrightarrow{\text{CH}_3OH, \text{rt}} R' - NO
\]

To the mixture of Oxone® (2 mol-equiv) and iodobenzene (1 mol-equiv) in MeOH (5 mL), an appropriate amide 6a-k (1 mmol) was added under stirring at room temperature. The reaction mixture was stirred at room temperature for 7-12 h (the reaction was monitored by GC-MS). After completion of the reaction, the solvent was evaporated under vacuum. The resulting residue was diluted with H₂O (10 mL), and extracted with EtOAc (3x10 mL). The organic phase was separated, and dried over MgSO₄ (anhydrous). Evaporation of EtOAc under reduced pressure afforded a final product which in case of crystalline products was additionally purified by recrystallization from CHCl₃/hexane.

**Methyl N-isopropylcarbamate 7c.**

![Methyl N-isopropylcarbamate](image)

Reaction of isobutyramide 6c (0.087 g, 1 mmol) according to the general procedure afforded 0.111 g (95%) of product 7c, isolated as an oil. ¹H NMR 500 MHz (CDCl₃): δ 1.15 (d, J=6.3 Hz, 6H, 2CH₃), 3.65 (s, 3H, COOC₃H₃), 3.81 (br s, 1H, CH), 4.55 (br s, 1H, NH). EI-MS m/z (relative intensity, %): 117 [M]+ (<5), 102 [M-CH₃]+(100), 86 [M-CH₂O]+(5), 70 [C₅H₄NO]+ (6), 59 [C₂H₅O₂]+ (26), 58 [C₃H₈N]+ (50).

**Methyl N-cyclobutylcarbamate 7d.**

![Methyl N-cyclobutylcarbamate](image)

Reaction of cyclobutanecarboxamide 6d (0.099 g, 1 mmol) according to the general procedure afforded 0.119 g (92%) of product 7d, isolated as an oil. ¹H NMR 300 MHz (CDCl₃): δ 1.62-1.71 (m, 2H), 1.81-1.88 (m, 2H), 2.27-2.32 (m, 2H), 3.64 (s, 3H, COOCH₃), 4.13-4.18 (m, 1H, CH), 4.89 (br s, 1H, NH). EI-MS m/z (relative intensity, %): 128 [M-1]+ 10), 110 (16), 95 [C₅H₅NO]+ (100), 81 [C₅H₇N]+ (13), 69 [C₄H₇N]+ (43), 55[C₄H₇]+ (32).

**Methyl N-cyclohexylcarbamate 7e.**

![Methyl N-cyclohexylcarbamate](image)

Reaction of cyclohexanecarboxamide 6e (0.127 g, 1 mmol) according to the general procedure afforded 0.140 g (89%) of product 7e, isolated as a slightly yellow microcrystalline solid, mp 73.5-74.5 °C (lit.², mp 72-75 °C). ¹H NMR 500 MHz
(CDCl₃): δ 1.09-1.20 (m, 3H), 1.31-1.38 (m, 2H), 1.58-1.62 (m, 1H), 1.67-1.72 (m, 2H), 1.92-1.94 (m, 2H), 3.48 (br s, 1H, CH₃), 3.65 (s, 3H, COOCH₃), 4.56 (br s, 1H, NH).

**Methyl N-(1-adamantanyl)carbamate 7f.**

![Structure of Methyl N-(1-adamantanyl)carbamate](image)

Reaction of 1-adamantanecarboxamide 6f (0.179 g, 1 mmol) according to the general procedure afforded 0.188 g (90%) of product, isolated as a microcrystalline solid, mp 118-120 °C (lit.3, mp 120 °C). ¹H NMR 300 MHz (CDCl₃): δ 1.67 (s, 6H), 1.93 (s, 6H), 2.07 (s, 3H), 3.60 (s, 3H, COOCH₃), 4.54 (br s, 1H, NH).

**Methyl (1-Boc-pyrrolidin-2-yl)carbamate 7g.**

![Structure of Methyl (1-Boc-pyrrolidin-2-yl)carbamate](image)

Reaction of 1-Boc-L-prolinamide 6g (0.214 g, 1 mmol) according to the general procedure afforded 0.183 g (75%) of product 7g, isolated as an oil. ¹H NMR 300 MHz (CDCl₃): δ 1.44 (s, 9H, COOC(CH₃)₃), 1.81-1.84 (m, 2H), 2.34-2.38 (m, 2H), 3.16 (br s, 2H), 3.68 (s, 3H, COOCH₃), 4.63 (br s, 2H, NH and CH). ¹³C NMR 75 MHz (CDCl₃): δ 21.02, 28.62 (COOC(CH₃)₃), 33.21, 46.74, 51.88 (COOCH₃), 79.43, 83.04, 174.02, 179.51.

**Methyl N-benzylcarbamate 7h.**

![Structure of Methyl N-benzylcarbamate](image)

Reaction of 2-phenylacetamide 6h (0.135 g, 1 mmol) according to the general procedure afforded 0.160 g (97%) of product 7h, isolated as a microcrystalline solid, mp 63-65 °C (lit.4, mp 64-65 °C). ¹H NMR 300 MHz (CDCl₃): δ 3.69 (s, 3H, COOCH₃), 4.36 (s, 2H, -CH₂-), 5.09 (br s, 1H, NH), 7.28-7.34 (m, 5H, Ph).

**Methyl N-(4-methylbenzyl)carbamate 7i.**

![Structure of Methyl N-(4-methylbenzyl)carbamate](image)

Reaction of 2-(p-tolyl)acetamide 6i (0.149 g, 1 mmol) according to the general procedure afforded 0.166 g (93%) of product 7i, isolated as a white microcrystalline solid, mp 68-70 °C. ¹H NMR 300 MHz (CDCl₃): δ 2.33 (s, 3H, -CH₃), 3.69 (s, 3H, COOCH₃), 4.32 (s, 2H, -CH₂-), 4.98 (br s, 1H, NH), 7.12-7.19 (m, 4Harom.).

**Methyl N-(p-methoxybenzyl)carbamate 7j.**

![Structure of Methyl N-(p-methoxybenzyl)carbamate](image)

Reaction of 2-(4-methoxyphenyl)acetamide 6j (0.165 g, 1 mmol) according to the general procedure afforded 0.185 g (95%) of product 7j, isolated as a white microcrystalline solid, mp 73-74 °C (lit.5, mp 73-74 °C). ¹H NMR 300 MHz (CDCl₃): δ 3.68 (s, 3H, COOCH₃), 3.78 (s, 3H, -OCH₃), 4.28 (br s, 2H, -CH₂-), 4.97
Methyl N-[(1-naphthyl)methyl]carbamate 7k.

Reaction of 1-naphthaleneacetamide 6k (0.185 g, 1 mmol) according to the general procedure afforded 0.200 g (93%) of product, isolated as pale yellow microcrystalline solid, mp 84-86 °C (lit.⁶, mp 84-88 °C). ¹H NMR 300 MHz (CDCl₃): δ 3.68 (s, 3H, COOC₂H₃), 4.79 (br s, 2H, -CH₂-), 5.09 (br s, 1H, NH), 7.39-7.41 (m, 2H, ArH), 7.46-7.52 (m, 2H, ArH), 7.77-7.78 (m, 1H, ArH), 7.84-7.86 (m, 1H, ArH), 7.96-8.01 (m, 1H, ArH).

General procedure for preparation of 1,4-benzoquinones 10a-e from amides 8a-e.

To the mixture of Oxone® (2 mol-equiv) and iodobenzene (1 mol-equiv) in CH₃CN/H₂O (6 mL, 1:1, v/v), an appropriate amide 8a-e (1 mmol) was added under stirring at room temperature. The reaction mixture was stirred at room temperature for 7-12 h (the reaction was monitored by GC-MS). After completion of the reaction, the reaction mixture was diluted with H₂O (10 mL), and extracted with CHCl₃ (3x10 mL). The organic phase was separated, and dried over Na₂SO₄ (anhydrous). Evaporation of CHCl₃ under reduced pressure afforded a pure product 10.

1,4-Benzoquinone 10a.

Reaction of benzamide 8a (0.121 g, 1 mmol) according to the general procedure afforded 0.106 g (98%) of product 10a, isolated as an orange microcrystalline solid, mp 115-116 °C (lit.,⁷ mp 116 °C). ¹H NMR 300 MHz (CDCl₃): δ 6.78 (s, 4H). The same product was obtained in reaction with 4-methoxybenzamide 8e (0.102 g, 94%).
2-Methyl-1,4-benzoquinone 10b.

Reaction of \( o \)-toluamide 8b (0.135 g, 1 mmol) according to the general procedure afforded 0.122 g (100%) of product 10b, isolated as a yellow microcrystalline solid, mp 68-69 °C (lit.\(^7\), mp 69 °C). \(^1\)H NMR 300 MHz (CDCl\(_3\)): \( \delta \) 2.03 (s, 3H, -CH\(_3\)), 6.59 (s, 1H), 6.65-6.76 (m, 2H).

2-Chloro-1,4-benzoquinone 10c.

Reaction of 2-chlorobenzamide 8c (0.155 g, 1 mmol) according to the general procedure afforded 0.135 g (95%) of product 10c, isolated as a yellowish microcrystalline solid, mp 54-56 °C (lit.\(^7\), mp 55-56 °C). \(^1\)H NMR 300 MHz (CDCl\(_3\)): \( \delta \) 6.80 (d, \( J = 9.8 \) Hz, 1H), 6.91 (d, \( J = 9.8 \) Hz, 1H), 6.99 (s, 1H).

2-Methoxy-1,4-benzoquinone 10d.

Reaction of 3-methoxybenzamide 8d (0.151 g, 1 mmol) according to the general procedure afforded 0.134 g (97%) of product 10d, isolated as a slightly brown microcrystalline solid, mp 142-144 °C (lit.\(^7\), mp 144 °C). \(^1\)H NMR 300 MHz (CDCl\(_3\)): \( \delta \) 3.83 (s, 3H, -OCH\(_3\)), 5.95 (br s, 1H), 6.72 (br s, 2H).

4-Hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone 10e.

Reaction of 2,4,6-trimethylbenzamide 8f (0.163 g, 1 mmol) according to the general procedure afforded product 10e, isolated as a semisolid mass which on recrystallization from EtOH/water yields pure crystalline product 0.144 g (95%), mp 44.5-45.5 °C (lit.\(^8\), mp 45-46 °C). \(^1\)H NMR 300 MHz (CDCl\(_3\)): \( \delta \) 1.43 (s, 3H, 4-CH\(_3\)), 1.86 (s, 6H, 2,6-CH\(_3\)), 6.62 (br s, 2H).
3. Copies of $^1\text{H}$ and $^{13}\text{C}$ NMR spectra
Benzylamine hydrochloride 3•HCl (300 MHz, CDCl$_3$)
(±)-α-Phenylpropylamine 5 (300 MHz, CDCl₃)
Methyl N-isopropylcarbamate 7c (500 MHz, CDCl₃)
Methyl N-cyclobutylcarbamate 7d (300 MHz, CDCl₃)
Methyl N-cyclohexylcarbamate 7e (500 MHz, CDCl₃)
Methyl N-(1-adamantanyl)carbamate 7f (300 MHz, CDCl₃)
Methyl (1-Boc-pyrrolidin-2-yl)carbamate 7g (300 MHz, CDCl₃)
Methyl (1-Boc-pyrrolidin-2-yl)carbamate 7g (75 MHz, CDCl₃)
Methyl N-benzylcarbamate 7h (300 MHz, CDCl₃)
Methyl N-(4-methylbenzyl)carbamate 7i (300 MHz, CDCl₃).
Methyl N-(p-methoxybenzyl)carbamate 7j (300 MHz, CDCl₃)
Methyl N-[(1-naphthyl)methyl]carbamate 7k (300 MHz, CDCl₃).
1,4-Benzooquinone 10a (300 MHz, CDCl₃)
2-Methyl-1,4-benzoquinone 10b (300 MHz, CDCl₃)
2-Chloro-1,4-benzoquinone 10c (300 MHz, CDCl₃)
2-Methoxy-1,4-benzoquinone 10d (300 MHz, CDCl₃).
4-Hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone 10e (300 MHz, CDCl₃)
References


